Remarks/Arguments

In response to the Office Action:

- Claims 1, 6, 12, 21, 29 and 37 have been amended.
- Claims 11, 23, 24, 25, 27 and 33-36 have been cancelled.
- Claim 26 stands withdrawn.

Restriction Requirement

Applicants affirm their election of Group V in response to the restriction requirement. Applicants also elect Compound 8 in table 1 as the species.

Applicants have amended the claims to comply with the restriction requirement, Claim 1 has been amended and Claims 23 24 and 33-35 have been cancelled. Claim 26 stands withdrawn pending possible rejoinder on allowance of the product claims (see request herein below).

Claim Rejections – 35 USC §112, Second Paragraph

Claims 1, 6, 7, 10-13, 18, 21, 22, 25, 27, 29, 31-33, 36, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 1 recites the limitation of "prodrug", which the Examiner says has indefinite metes and bounds because it is not clear where the functional group for a "prodrug" would be. In response to this rejection, the word "prodrug" has been deleted from Claims 1, 29 and 37. Claim 25 which provided a specific embodiment of a prodrug has been cancelled.

b. The Examiner states Claim 1 recites the phrase "any aryl, heteroaryl or heterocyclyl group in a substituent on R^{5}" in the middle of the definition of R^{70}, which makes it unclear if R^{5} optionally has additional substituents or if R^{70} optionally has additional substituents. In response to this rejection Applicants have amended the objected to phrase read "and any aryl, heteroaryl or heterocyclyl group in a R^{70} group" to further clarify the meaning. This phrase is already used in Claim 1 and has not be rejected by the Examiner.

c. Claim 1 also recited many limitations in parentheses, which the Examiner said was unclear if they are part of the claim, or a mere explanation. In response to this rejection Applicants have deleted numerous parentheses in Claims 1 and 6 and replaced them, where appropriate, with commas.

d. The Examiner said Claim 6 lacks antecedent basis because it depends on claim 1, but recites the limitation of "NR^7R^8" for R^1-R^4, which is not recited in claim 1. In response to this rejection, "NR^6R^7" has been deleted from claim 6. The definitions of R^6 and R^7 have also been deleted.

e. Claim 10 recites the phrase of "R^9 includes a methylene group...", which the Examiner said was unclear as to which group in claim 1 is intended for R^9 since many of the groups could have a "methylene" group. In response to this rejection the phrase "and R^9 includes a methylene group directly adjacent to X^1" has been deleted from Claim 10.

f. The Examiner said Claim 11 lacks antecedent basis because it depends on claim 1, but recites X^1R^9 "which includes a bridging alkylene,...", which is not recited in claim 1. Claim 11 has been deleted rendering this rejection moot.

g. Claims 7, 12, 13, 18, 21, 22, 25, 27, 29, 31-33, 36, and 37 are rejected by the Examiner as being dependent on claim 1, carrying over the indefinite limitations. Applicants consider the amendments listed herein above overcomes this rejection.

Claim Rejections – 35 USC §112, First Paragraph

Claims 1, 25, 27, 29, 36, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, the limitation of "prodrug" in said claims does not have adequate written description. As stated above, Applicants have deleted the word "prodrug" from the claims. Applicants therefore believe that this rejection has been overcome.

Claim Rejections – 35 USC §112

Claims 27 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the Examiner states that the specification, while being enabling for a method of treating colorectal or breast cancer, does not reasonably provide enablement for a method of treating "hyperproliferative disease", or cancer in general. The Examiner says that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Whilst Applicants do not agree with the Examiner position on this, Applicants have deleted these two claims to expedite prosecution.

Claim Rejections – 35 USC §103

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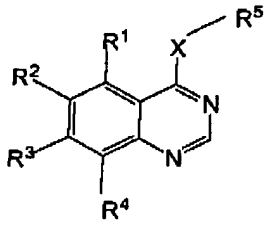
Claims 1, 6, 7, 10, 12, 13, .8, 21, 27, 29, 31, 33, 36 and 37 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Myers et. al. (US 5,721,237).

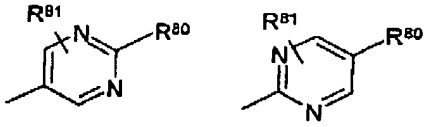
Applicants disagree and respectfully point out that the Examiner has reached this conclusion with the advantage of hindsight.

The present invention provides aurora kinase inhibitors of formula (I):



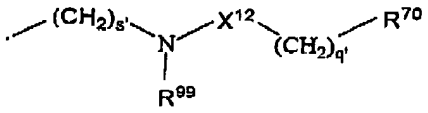
(I)

wherein R^5 is pyrimidine substituted in a para position (relative to the quinazoline ring), i.e.:



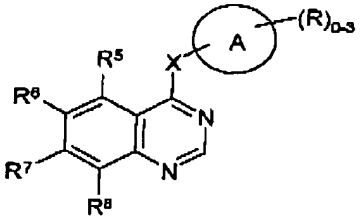
(iii) or (v)

by a substituent R^{80} of formula (II):



(II)

Myers et al. provides compounds of formula (I')



(I')

wherein A is a mono- or bi-cyclic aryl, heteroaryl, cycloalkyl or heterocycloalkyl ring system (col. 3 line 24-28).

If we look at the definitions of these terms (col. 3 line 45 to col. 4 line 10 and col. 4 line 31 to line 49), it can be seen that A can, in fact, be selected from a large number (36) of cyclic systems:

Monocyclic aryl or heteroaryl:

phenyl (3)	pyrrolyl (3)	thienyl (3)
furyl (3)	thiazolyl (2)	imidazolyl (2)
pyrazolyl (2)	pyridyl (4)	pyrazinyl (3)
pyrimidinyl (2)	pyridazinyl (3)	isothiazolyl (2)
isoxazolyl (2)	oxazolyl (2)	

Bicyclic aryl or heteroaryl:

naphthyl (7)	tetralinyl (7)	1,2,3,4-tetrahydroquinolinyl (6)
benzofuryl (5)	benzothienyl (5)	indolyl (5)
indolinyl (5)	1,3-benzodioxolyl (4)	benzodioxanyl (5)
quinolinyl (6)	tetrahydroquinolinyl (6)	isoquinolinyl (6)
quinazolinyl (5)	quinoxalinyl (5)	

Monocylic cycloalkyl:

cyclopentyl (2)	cyclohexyl (3)	cycloheptyl (4)

Bicyclic cycloalkyl:

decalinyl (7)

Monocyclic heterocycloalkyl:

piperdinyl (4)	piperazinyl (3)	morpholinyl (2)

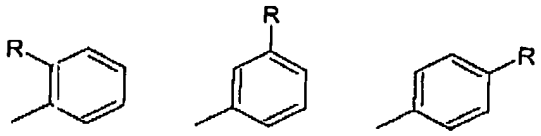
Bicyclic heterocycloalkyl:

decahydroquinolinyl (6)

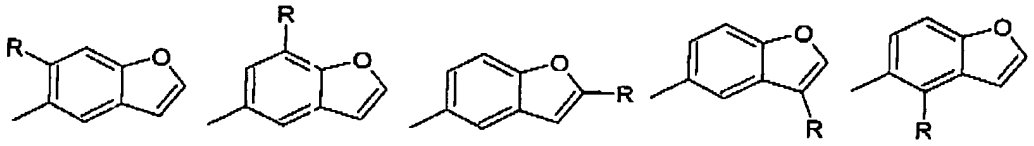
From this large list, preferred ring systems are disclosed as phenyl, pyridyl, thienyl, furyl, pyrazolyl, naphthyl, tetralinyl, 1,2,3,4-tetrahydroquinolinyl, indolyl, indolinyl, quinolinyl, tetrahydroquinolinyl, cyclohexyl, piperdinyl and piperazinyl (col 4, lines 51-55); and more preferred ring systems are phenyl, naphthyl and indolyl (col 4, lines 63-64).

In order to arrive at the present invention, the skilled person, starting from Myers et al., must first select pyrimidinyl from this list of 36 rings, ignoring all of the suggestions as to which rings are preferred.

Following this choice, the skilled person must then consider R. For each ring substituted with R, a number of positional isomers will exist. For example if A is phenyl, R may be positioned as follows:



or if A is benzofuran, there are 5 possible positions for R:



An approximate number of these positional isomers follows each ring type listed above in brackets. If this variation is taken into account then the skilled person is faced with approximately 144 possible options for A.

Our invention relates to only one of these options i.e. that A is pyrimidinyl and that it is substituted in a position that is para to the quinazoline ring.

Turning now to R, Myers et al. provides that this can be selected from a list of at least 22 possible substituents :

hydrogen	phenyl	aralkyl
alkyl	halophenyl	hydroxy

alkoxy	mono- alkylamino	di-alkylamido
aryloxy	di-alkylamino	alkylthio
acyloxy	acylamino	alkylsulfinyl
halo	carboxy	alkylsulfonyl
haloalkyl	amido	
amino	mono-alkylamido	

wherein hydrogen, alkyl, alkoxy, halo, haloalkyl, alkythio, alkylsulfinyl, alkylsulfonyl, phenyl and aralkyl are preferred (col 4, lines 57-8) and hydrogen, methoxy, ethoxy, chloro, trifluormethyl, methylsulfonyl, phenyl and benzyl are more preferred (col 4, lines 66-7).

Our invention requires that the skilled person select the non-preferred acylamino substituent from this list of 22.

If the skilled person selected A and R as described above, he would be choosing a single very specific combination from a very large number of possible options. A very basic quantitative assessment reveals that there are over 3000 possible options.

The Examiner is respectfully reminded of section 2141 of the MPEP under the heading "II. Basic Considerations Which Apply To Obviousness Rejections" where it is stated:

When applying 35 USC 103, the following tenets of patent law must be adhered to:
(A) The claimed invention must be considered as a whole;
(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
(D) Reasonable expectation of success is the standard with which obviousness is determined.
Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986). (emphasis added)

What would prompt the skilled person to make this particular selection of one combination of groups from over 3000 possible options given in Myers *et. al.*? Why would (s)he expect the combination to be successful? There is nothing in Myers *et. al.* that would motivate the skilled person to make this choice.

Pyrimidinyl is not a preferred ring, the para position is not a preferred substituent position and acylamino is not a preferred substituent. Applicants believe that the Examiner has applied a significant degree of impermissible hindsight in deriving our invention from the generic disclosure of Myers whilst ignoring the preferred embodiments of that disclosure.

In addition it should also be noted that the compounds of the invention are selective for aurora A kinase over other kinases, and in particular over tyrosine kinases such as EGFR (epidermal growth factor receptor). Given well established case law such as In re Papesch (137 USPQ 43) which requires the Examiner to give consideration to the pharmacological properties of the compounds being claimed, for this additional reason a 35 USC 103 rejection based on Myers *et. al.* is not properly sustainable.

The above amendments have been made without prejudice to Applicants right to prosecute any cancelled subject matter in a timely filed continuation application.

Applicants believe the application is in condition for allowance, which action is respectfully requested.

Applicants further request rejoinder of the process claim, claim 26, finding basis in the MPEP at section 821.04(b) under Rejoinder of Process Requiring an Allowable Product where it is stated that:

... if applicant elects a claim(s) directed to a product which is subsequently found allowable, withdrawn process claims which depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must depend from or otherwise require all the limitations of an allowable product claim for that process invention to be rejoined. Upon rejoinder of claims directed to a previously nonelected process invention, the restriction requirement between the elected product and rejoined process(es) will be withdrawn.

Applicants believe that the present circumstances fulfill this set of criteria and respectfully request that the process claim, claim 26, is rejoined.

A petition for a 1 month extension of time is being filed herewith, the Commissioner is hereby authorized to charge any deficiency in the fees or credit any overpayment to deposit account No. 50-3231, referencing Attorney Docket No. Z70598-1P US.

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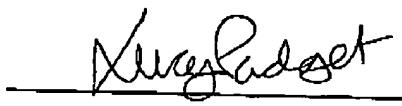
Although Applicants believe no excess claim fees are due, the Commissioner is hereby authorized to charge any deficiency in the fees or credit any overpayment to deposit account No. 50-3231, referencing Attorney Docket No. Z70598-1P US.

Respectfully submitted,



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Enclosures: Transmittal Form
Fee Transmittal Form
Petition of 1-month extension of time